Assessment of carotid calcifications on digital panoramic radiographs

Monteiro, I A; Ibrahim, C; Albuquerque, R; Donaldson, N; Salazar, F; Monteiro, L

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Corresponding Author: Dr. Carlos Ibrahim, DDS,MClinDent

Corresponding Author's Institution: Guys Hospital NHS Foundation Trust

First Author: Ines Alves Monteiro, Msc

Order of Authors: Ines Alves Monteiro, Msc; Carlos Ibrahim, DDS,MClinDent; Rui Albuquerque, DDS, MS, FHEA, PhD; Neil Donaldson, BDS,MFDS,PgDip; Filomena Salazar, PhD,DDS; Luis Monteiro, PhD,MSc,DDS

Abstract: Objectives: To assess the validity of digital panoramic radiographs as an effective means of diagnosis for atherosclerosis and as a potential aid in the early detection of the disease. Study Design: We reviewed 2014 digital panoramic radiographs taken throughout 2012 and 2013 to identify the presence of calcified atherosclerotic plaques of both female and male patients all aged over 18 years. In addition the medical records of these patients were reviewed in order to establish if there were any predisposing risk factors for atherosclerosis presentation. Statistical analysis was performed to identify any possible link between radiographic atherosclerotic plaques and predisposing risk factors for atherosclerosis using univariate and multivariate models. Statistical significance criteria was defined as $p < 0.05$. Results: Out of 2014 patients (1149 female and 865 male), 191 (9.5%) were determined to have calcified atherosclerotic plaques on panoramic radiography. There was a statistically significant relationship between the presence of calcified atherosclerotic plaques and the established risk factors of atherosclerosis such as gender (OR = 2.39, $p < 0.001$), age (OR = 1.5, $p < 0.001$), stroke (OR = 5.38, $p < 0.001$) and hypertension (OR = 2.11, $p < 0.001$). Conclusion: To our knowledge this is the largest study investigating atherosclerotic plaques on digital panoramic radiographs ever carried out in Portugal. Dental practitioners need to be aware of these incidental findings and to consider referring these patients for further investigations to confirm diagnosis.

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Short title: Assessment of carotid calcifications on Digital Panoramic Radiographs

Authors: Inês Alves Monteiro[1], Carlos Ibrahim[2], Rui Albuquerque[3], Neil Donaldson[3], Filomena Salazar[1], Luis Monteiro[1]

1. Medicine and Oral Surgery Department and Institute of Research and Advanced Training in Health Sciences and Technologies (IINFACTS), University Institute of Health Sciences (IUCS-N), CESPU, 4585-116 Paredes, Portugal
2. Guys Hospital, Oral Surgery Department, Great Maze Pond, London, SE1 9RT
3. Birmingham Dental Hospital/ School of Dentistry, University of Birmingham, Birmingham B4 6NN, UK

Corresponding author:

Dr Carlos Ibrahim

Guys Hospital NHS Foundation Trust

Oral Surgery Department

Great Maze Pond,

London

SE1 9RT

Email: Ibrahim_777@hotmail.com

Phone: 020 7188 8006

Fax: 020 7188 8006

SUMMARY

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Results: Out of 2014 patients (1149 female and 865 male), 191 (9.5%) were determined to have calcified atherosclerotic plaques on panoramic radiography. There was a statistically significant relationship between the presence of calcified atherosclerotic plaques and the established risk factors of atherosclerosis such as gender (OR = 2.39, $p < 0.001$), age (OR = 1.5, $p < 0.001$), stroke (OR = 5.38, $p < 0.001$) and hypertension (OR = 2.11, $p < 0.001$).

Conclusion: To our knowledge this is the largest study investigating atherosclerotic plaques on digital panoramic radiographs ever carried out in Portugal. Dental practitioners need to be aware of these incidental findings and to consider referring these patients for further investigations to confirm diagnosis.

Keywords: Atherosclerosis, digital panoramic radiographs (DPR), cardiovascular disease, radiography.

INTRODUCTION

Cerebral Vascular Accidents (CVA) are the third greatest cause of death in industrialized countries (1), being considered one of the greatest public health problems due to their high incidence and the cost of physical and psychological rehabilitation of patients (2). There are

two types of CVA: hemorrhagic which occurs when there is rupture of a blood vessel in the brain and ischemic occurring due to the obstruction of arteries due to thrombosis (3).

When atherosclerosis occurs in arteries that supply blood to the brain, namely the carotid arteries, it can lead to a CVA, and when atherosclerosis develops in the arteries that supply blood to the heart a myocardial infarction may occur resulting in thousands of deaths annually (1,4).

Atherosclerosis is a chronic inflammatory disease associated, in part, with aging. It is characterized by narrowing and loss of elasticity of blood vessels, in which fatty deposits, called atheromas, adhere to the inner layers of arteries which in turn reduce blood flow (4). The calcified atheromas are composed of lipids, calcium and fibrous tissue (5). They start forming following the deposition of small cholesterol crystals that subsequently grow in size and volume, leading to increased calcium deposition and production of fibrous tissue by fibroblasts causing hardening of the arteries and resulting in the formation of the atheroma (6).

The presence of calcifications in the lateral areas of the soft tissues of the neck (especially in the bifurcation of the internal and external carotid arteries, located laterally and inferiorly to the hyoid bone) in maxillofacial images has received special attention since they were first observed and reported in 1981 (3).

There are several predisposing factors for atherosclerosis, many of which are similar to those associated with stroke. These include diabetes mellitus, obesity, hypercholesterolemia, hypertension, alcoholism, smoking status, menopause and history of cardiovascular disease (4,6).

In digital panoramic radiographs (DPRs), atherosclerotic calcifications of the carotids are described as a nodular and heterogeneous mass, independent of the hyoid bone and epiglottis, situated below, above or between the spaces of the intervertebral discs C3 and C4 or at a 45° angle to the angle of the jaw (1, 2). The diagnosis of atherosclerotic calcification by DPR requires acuity and experience on the part of the clinician, since it is possible to have false positives due to the proximity of radiopaque anatomical structures such as the triticeous cartilage (4).

Dentists frequently prescribe and report on DPRs and therefore are well placed to identify possible atherosclerotic plaques. Consequently, we intend to investigate more fully the relationship between atherosclerotic plaque on DPR and risk factors for atherosclerosis, to consider this as a possible aid to diagnosis.

MATERIAL AND METHODS

We performed a retrospective descriptive analysis of 3843 patients (all patients seen in "Clinical Nova Saúde de Gandra" in the years 2012 and 2013). "Clinical Nova Saúde de Gandra" receives patients from the Oporto community who are self referred or referred by General Practitioners (GP) or General Dental Practitioners (GDP) to this Central University Clinic. Inclusion criteria consisted of individuals of both genders, aged over 18, who had undergone high quality DPR investigation, where the field included the cervical vertebrae and who had completed a screening form. Exclusion criteria were individuals under the age of 18, DPRs of poor resolution or which did not include the cervical vertebrae, clinical files with incomplete screening forms, and cases with unclear or missing data.

Prior ethical approval was obtained for the use and analysis of all clinical cases of patients for the years 2012 and 2013. The study was performed in full accordance with the World Medical Association Declaration of Helsinki. Data collection involved review of the patient's clinical record, where the following data was extracted: name, case number, age and gender. Later, after analysis of the screening form, data was collected related to diseases such as hypertension, hypercholesterolemia, diabetes, stroke, smoking and alcohol. Finally, we proceeded to the review the DPRs.

The DPRs were reviewed by two independent practitioners. Where there was disagreement, the practitioners would review DPRs together and reach consensus. Training and calibration was carried out before the x-ray analysis. The Kappa coefficient achieved by the practitioners was 0.8.

This study used DPRs performed using an Ortopantomographer Vatech Pax-400C and viewed with the digital program Easy Dent V4 Viewer 4.1.5.1. This programme offers manipulation of contrast and density, allowing for better analysis of the atheromatous plaques. We aimed to identify patients with atherosclerosis, who presented with plaques of

calcified atheroma in the bifurcation area of the carotids. A positive finding of atherosclerotic calcifications was considered if one or more nodular and heterogeneous masses were present, independent of the hyoid bone and epiglottis, located immediately below, above or between the spaces of the intervertebral discs C3 and C4 or at an angle of 45 degrees to the angle of the jaw (Figure 1).

Statistical analysis included descriptive statistical measures (frequencies, means and measures of dispersion) and inferential statistics (comparison of means and association between variables). Prior to the selection of statistical tests, the assumptions of the tests were checked. Specifically for comparing ages between subjects with and without atherosclerosis, the Student's t test for independent samples was used. For this purpose, we combined using the Shapiro-Wilk test (which tests whether the distribution of the variable of interest is significantly different from normal distribution) with the visual inspection of the histogram and asymmetry values (Sk) and kurtosis (K). Where the results were deemed not to be normally distributed, we proceeded to use the alternative non-parametric Mann-Whitney test. To calculate the significance of the association between each of the variables and the presence of atherosclerosis, we used contingency tables. To test whether the differences between groups were statistically significant regarding each of the variable under study, chi-square tests were used if they met the test assumptions (ie, the number of expected observations is less than 5 or 20% of all observations). Where we could not validate assumptions, we proceeded to use the Fisher test for determination of statistical significance. Finally, we proceeded to the construction of a multivariate model to test: 1) if the combination of the above variables significantly predicts the presence / absence of atherosclerosis; 2) which variables have a statistically significant relationship with the presence / absence atherosclerosis. To this end, we conducted a binary logistic regression model in which the variables gender, age, alcohol consumption, smoking, diabetes, stroke, hypertension and hypercholesterolemia were introduced as independent variables and atherosclerosis as the dependent variable. The multivariate model allows testing of the association of each variable with the dependent variable, taking into account all other variables. Statistical analysis was performed using the IBM SPSS software (version 24). Statistical significance was defined as $p < 0.05$.

RESULTS

From an initial sample of 3843 individuals, a final sample of 2014 was reached with 1,149 female and 865 males, aged between 18 and 90 years (mean = 42.23, SD = 15:41). 1829 cases were excluded due to; age under 18, lack of information, low resolution or not showing the relevant area of the DPR previously described and required for the diagnosis of atheroma plaques.

The sample was mainly composed of people who did not consume alcohol (65.2%) and did not smoke (71.4%). Among the medical conditions evaluated (i.e., diabetes, stroke, hypertension and hypercholesterolemia), hypertension was the most common condition (12.6%), in contrast to the CVA with a frequency of only 0.4%. The sample characteristics are summarized in Table 1.

Of these 2014 subjects, 191 (9.5%) were found to have atherosclerosis. We analysed possible relations of detected atherosclerosis with other clinical variables. The mean age of subject with atherosclerosis was higher (mean = 53.98 ± 14.60), relative to those without (mean = 41.10 ± 14.99). We found that there were significant differences between the groups (Mann-Whitney test, $Z = -10.54$, $p < 0.001$).

By analyzing the significance of the chi-square test, we observed that gender and smoking had a statistically significant association with the atherosclerosis. Specifically, with regard to gender, the contingency table demonstrates the existence of a significantly higher prevalence of cases in female participants ($X^2_{(1)} = 12.52$; $p < 0.001$). A statistically significant relationship between the atherosclerosis and tobacco use was demontrated ($X^2_{(1)} = 5.22$, $p = 0.022$), which suggested smokers have a lower frequency of atherosclerosis. Furthermore, there was no significant relationship between alcohol consumption and the presence of atherosclerosis in the present sample (Table 2).

Regarding the association between clinically relevant risk factors and the presence / absence of atherosclerosis on DPR, all studied risk factors (diabetes, stroke, hypertension and hypercholesterolemia) had statistically significant relationships with atherosclerosis in univariate analysis, suggesting each of these diseases is associated with increased prevalence of atherosclerosis on radiograph (Table 3).

Finally, through the use of multivariate binary logistic regression, using the combination of the variables gender, age, smoking, alcohol, diabetes, stroke, hypertension and hypercholesterolemia, it was found that the variables gender (OR = 2.39, p <0.001), age (OR = 1.5, p <0.001), stroke (OR = 5.38, p <0.001) and hypertension (OR = 2.11, p < 0.001) were statistically significant predictors of the presence of atherosclerosis (Table 4). Thus, it can be suggested that females have a greater risk of radiographic presentation of atherosclerosis than men, and that an increase in age is associated with an increased risk of developing this condition. This is also true for stroke and hypertension, suggesting that the presence of these conditions is associated with a higher incidence of having atherosclerosis detected on DPR.

DISCUSSION

Several studies have described a usefulness of DPR in detecting vascular diseases such as carotid atherosclerosis with a relative high sensibility and specificity (7,8). Khambet et al. (8) reported values for sensitivity of 76% and specificity of 99% for DPR detecting calcified carotid artery atheromatous plaques. With this in mind we aimed to analyse the relation between atherosclerotic plaque detected by DPR and risk factors for atherosclerosis and related diseases.

The recognition of atheroma on DPR nonetheless has limitations, such as quantifying the degree of stenosis and arterial obliteration, as well as detecting non calcified atherosclerotic lesions. Consequently Doppler ultrasound is still the main diagnostic test of this pathology, being affordable, accurate and non-invasive (1,9-11). Nevertheless, DPR is common in dental medicine clinics offering an alternative opportunity for diagnosis of atherosclerosis. Further studies are required to evaluate the level of concordance between the DPT and ultrasound findings with a representative sample and blinded examiners.

Regarding the prevalence of calcifications of the carotid arteries on the DPT, the literature shows some variance. A study conducted by Dorado *et* al. (11) obtained a prevalence of 15.5%, Ertas and Sisman (12) obtained a prevalence of cases of 66% in contrast to a study of Bryam *et* al. (6) who obtained results of 2.1%. This present study had a total prevalence of 9.5%. The disparity of results reported could be due to the difficult diagnosis of calcifications through DPT, since although the dentist is able to describe and identify the alveolar bone, temporomandibular, maxillary, mandibular and cervical regions, often dentists feel less

confident reporting on the cervical region (1). In addition, the differential diagnosis of calcifications includes anatomical radiopacity (hyoid bone, styloid process, calcified hyoid ligament, calcified thyroid cartilage, triticeous cartilage, epiglottis, earlobe, soft palate, tongue and anterior tubercle of the first cervical vertebrae-atlas) and pathological radiopacity (lymph nodes, sialoliths of the submandibular gland, loose bodies, calcified acne and tonsilloliths) (1,4).

The risk factors for atherosclerosis, according to the literature, coincide with cardiovascular disease (13), such as increasing age (14), history of stroke, hypertension, diabetes, smoking, hypercholesterolemia (1,6,9,11,12,14), alcohol consumption (4,15) and obesity (16). Zheng *et* al. (15) reported statistical significance between alcohol consumption in a population with atherosclerosis and cardiovascular accidents. Regarding diabetes, some authors found a relationship with the disease (17,18) but others studies have not (9,12). In the present study no statistical significance was found in relation to diabetes, cholesterol and alcohol when variables were adjusted. This could indicate that possible relation between atherosclerosis detected in DPR and these diseases are weak or simply this could be a result of a sampling bias.

We found a relationship of calcified carotid artery atheromatous plaques detected by DPR with both arterial hypertension and stroke. Moshfeghi *et* al. (19) report a statistically significant relationship between hypertension and atherosclerotic calcifications, with a prevalence of 26% in total. Atalay *et* al. (9) found also an association with hypertension. Ertas and Sisman (12) found a statistically significant association between prevalence of calcifications and history of stroke and hypertension, consistent with the results of our study. Griniatsos *et* al. (3) concluded in their study that patients with a history of stroke and calcifications in the carotid detected by DPR incur a greater risk of further cardiovascular events in the future, therefore it may be inferred that patients whose carotid arteries are likely to have calcifications, may be at risk of stroke.

With regard to smoking, the results showed that those who smoke are less affected by atherosclerosis although without significance in multivariate analysis. This may be due, once again, to sample bias or recall bias. In the literature there is no consensus regarding this association, with some articles demonstrating a relationship between smoking and carotid atheromas detected by DPR (14) and others not reaching statistical significance (9).

According to several studies, atherosclerotic lesions of carotid arteries tend to be more common in women and tend to increase from the age of 18, with a higher incidence of cases from 55 years old (2,7,8,14,20-22). This is consistent with our findings which showed statistical significance with these two variables.

Overall, our results show that patients with calcifications in the carotid arteries detected by dental panoramic radiographs are associated with risk factors such hypertension, older age and are therefore at a higher risk of CVA. Detection and referral of these patients for further investigations could be beneficial in prevention and management of this disease. Furthers studies with larger samples should be performed not only to determine better methods of early diagnosis of this disease with more sensitivity but also to better understand the relationship of this diagnosis to other systemic diseases such as diabetes, renal failure or even periodontitis (23,24).

In conclusion, dentists need to recognise the relevance of this incidental finding on DPR, as early detection of these calcifications can aid the diagnosis of atherosclerosis. However, as this is a difficult diagnosis, due to anatomical variations and pathological conditions that may exist, some training and calibration would be recommended.

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Legend of figures

Figure 1 – Image of digital panoramic radiograph (DPR) of a male patient with 65 year-old showing small calcifications on the left side of the DPR.

Figure

Click here to download high resolution image

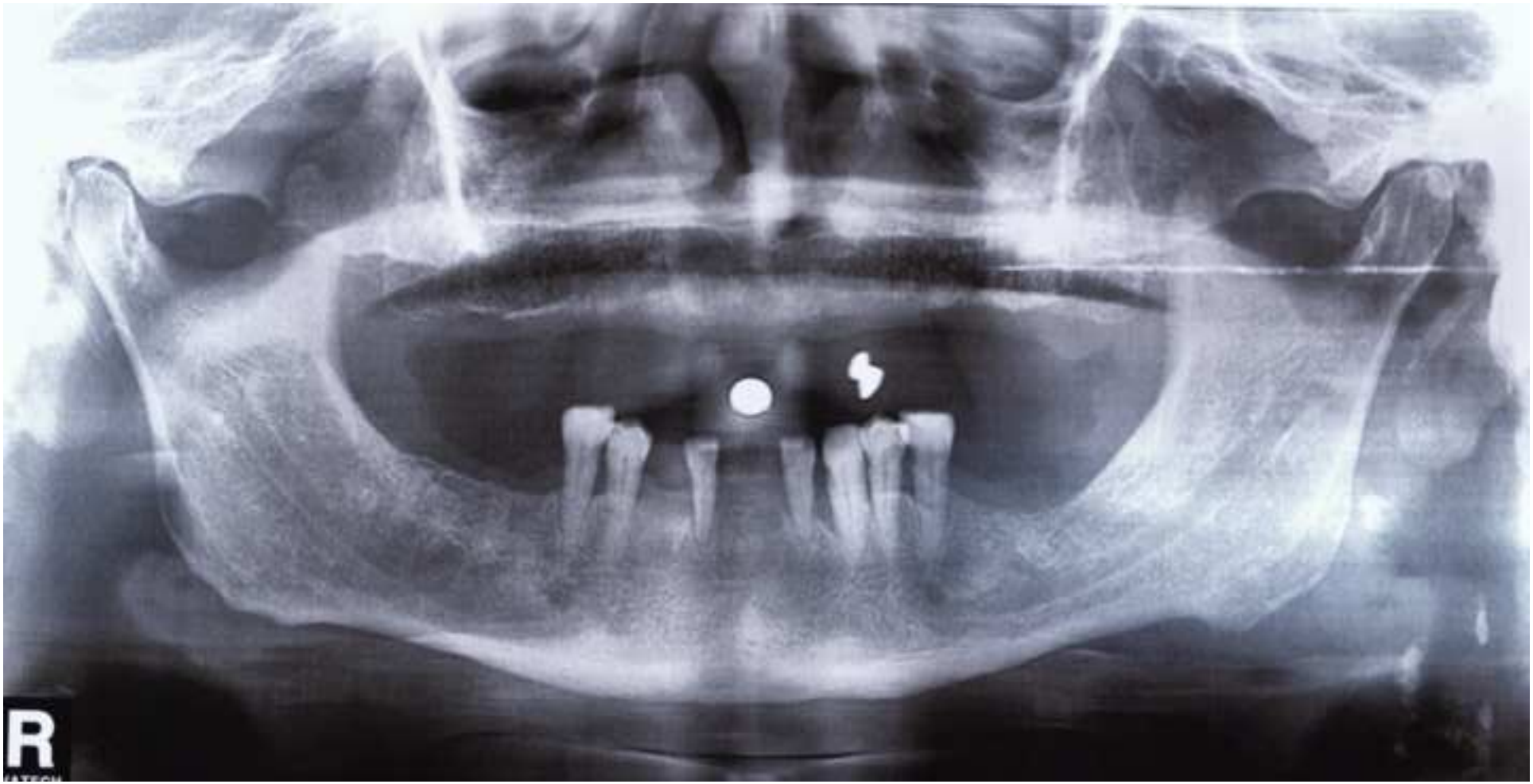

Table 1. Sample characteristics

		Control Group (n=1823)	Artherosclerosis Group (n=191)	Total (n=2014)
Gender				
	Female	1017 (55.8%)	132 (69.1%)	1149 (57.1%)
	Male	806 (44.2%)	59 (30.9%)	865 (42.9%)
Age mean (standard deviation)		41.10 (14.99)	53.98 (14.60)	43.23 (15.41)
Smoker				
	No	1280 (70.2%)	147 (78.6%)	1427 (71.4%)
	Yes	531 (29.1%)	40 (21.4%)	571 (28.6%)
Alcohol				
	No	1195 (65.6%)	118 (61.8%)	1313 (65.2%)
	Yes	628 (34.4%)	73 (38.2%)	701 (34.8%)
Diabetes				
	No	1727 (98.4%)	164 (85.9%)	1891 (93.9%)
	Yes	95 (5.2%)	27 (14.1%)	122 (6.1%)
CVA				
	No	1819 (99.8%)	187 (97.9%)	2006 (99.6%)
	Yes	4 (0.2%)	4 (2.1%)	8 (0.4%)
Hypertension				
	No	1633 (89.6%)	126 (66.0%)	1759 (87.4%)
	Yes	189 (10.4%)	65 (34.0%)	254 (12.6%)
Hypercholesterolemia				
	No	1781 (97.7%)	174 (91.1%)	1955 (97.1%)
	Yes	42 (2.3%)	17 (8.9%)	59 (2.9%)

CVA, cerebral vascular accidents;

Table 2

Table 1. Contingency tables: association between variables gender, smoking and alcohol habits and atherosclerosis.

			Artherosclerosis		Total	$X^2_{(gl)}$ p
			Não	Sim		
Gender	Female	Observed	1017	132	1149	
		Expected	1040	109	1149	
	Male	Observed	806	59	865	$X^2_{(1)}$= 12.52
		Expected	783	82	865	p < 0.001
	Total	Observed	1823	191	2014	
		Expected	1823	191	2014	
Smoker	Yes	Observed	531	40	571	
		Expected	517.6	53.4	571	
	No	Observed	1280	147	1427	$X^2_{(1)}$= 5.22
		Expected	1293.4	133.6	1427	p = 0.022
	Total	Observed	1811	187	1998	
		Expected	1811	187	1998	
Alcohol	Yes	Observed	628	73	701	
		Expected	634.5	66.5	701	
	No	Observed	1195	118	1313	$X^2_{(1)}$= 1.08
		Expected	1188.5	124.5	1313	p = 0.298
	Total	Observed	1823	191	2014	
		Expected	1823	191	2014	

X^2: Chi-Square statistic; gl: degrees of freedom.

Table 3

Table 1. Contingency tables: association between variables related to clinical conditions and the main variable - atherosclerosis

			Artherosclerosis			$X^2_{(gl)}$
			No	Yes	Total	p
Diabetes	Yes	Observed	95	27	122	
		Expected	110.4	11.6	122	
	No	Observed	1727	164	1891	$X^2_{(1)}$= 24.17
		Expected	1711.6	179.4	1891	p <0.001
	Total	Observed	1823	191	2014	
		Expected	1823	191	2014	
CVA	Yes	Observed	4	4	8	
		Expected	7.2413	0.7586	8	
	No	Observed	1819	187	2006	p =0.004 [a]
		Expected	1815.7587	190.2413	2006	
	Total	Observed	1823	191	2014	
		Expected	1823	191	2014	
Hypertension	Yes	Observed	189	65	254	
		Expected	229.9	24.1	254	
	No	Observed	1633	126	1759	$X^2_{(1)}$= 87.76
		Expected	1592.1	166.9	1759	p <0.001
	Total	Observed	1823	191	2014	
		Expected	1823	191	2014	
Hypercholesterolaemia	Yes	Observed	42	17	59	
		Expected	53.4	5.6	59	
	No	Observed	1781	174	1955	$X^2_{(1)}$= 26.46
		Expected	1769.6	185.4	1955	p <0.001
	Total	Observed	1823	191	2014	
		Expected	1823	191	2014	

CVA, cerebral vascular accidents; X^2: Chi-Square statistic; gl: degrees of freedom; a; Fisher's test due to the non verification of the assumptions required to perform the chi-square test

Table 4

Table 1. Multivariate binary logistic regression (dependent variable: presence / absence of atherosclerosis)

	C	SD	Wald	df	P Value	OR	CI 95% Lower limit	CI 95% Upper limit
Constant	3.006	1.912	2.470	1	0.116	20.198		
Gender[a]	0.870	0.188	21.500	1	0.000	2.387	1.653	3.448
Age	0.046	0.006	56.487	1	0.000	1.047	1.035	1.060
Smoker[b]	0.244	0.207	1.390	1	0.238	1.277	0.851	1.917
Alcohol[b]	0.216	0.178	1.484	1	0.223	1.242	0.877	1.759
Diabetes[c]	0.039	0.273	0.020	1	0.887	1.040	0.609	1.775
CVA[c]	1.683	0.790	4.537	1	0.033	5.383	1.144	25.331
Hypertension[c]	0.745	0.202	13.536	1	0.000	2.106	1.416	3.132
Hypercholesterolaemia[c]	0.379	0.342	1.229	1	0.268	1.460	0.748	2.852

CVA, cerebral vascular accidents; C: coefficient; SD: Standard Deviation; df: degrees of freedom; OR: odds ratio; CI Confidence interval 95%; [a]reference: male; [b]reference: absence of consuming; [c]reference: absence of condition.